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Concerning the following application:

ATTORNEY DOCKET NO.: 18396/2112

Application of:	Sattelle, et al.
Serial No.:	10/010,873
Filed:	December 7, 2001
Entitled:	RECOMBINANT NEMATODE NICOTINIC RECEPTOR AND USES

Examiner: Not Yet Assigned  
Group Art Unit: 1632  
Conf. No.: 7464

Facsimile No.: 1-703-746-9195

Our Facsimile No.: 1-617-227-4420

Number of pages including cover sheet: 7

Transmitted herewith: Transmittal Letter; Request for Corrected Filing Receipt; Copy of Page 1 of Application; Marked-Up Version of Official Filing Receipt

**CERTIFICATION**

I hereby certify that the paper identified above is being facsimile transmitted to the U.S. Patent and Trademark Office, on the date indicated below.

Date:

June 16, 2004

Barbara A. Gyure  
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Tel: 617-239-0100

Atty. Docket No.: 18396/2112

PATENT

## IN THE UNITED STATES PATENT AND TRADEMARK OFFICE


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**UNDER 37 C.F.R. § 1.6d**

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Brenda M. Woods

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P.O. Box 1450  
Alexandria, VA 22313-1450

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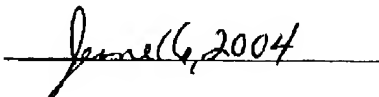
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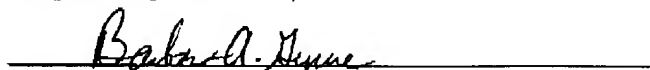
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Respectfully submitted,

Date:



  
Name: Barbara A. Gyure  
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PATENT

## IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

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Serial No.: 10/010,873  
Filed: December 7, 2001  
Entitled: RECOMBINANT NEMATODE  
NICOTINIC RECEPTOR AND USES

Examiner: Not Yet Assigned

Group Art Unit: 1638

Conf. No.: 7464

COPY

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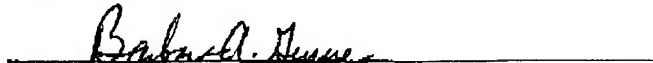
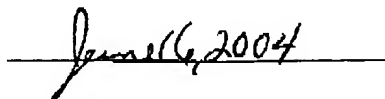
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Brenda M. Woods

Name of Person Faxing Paper



Signature of Person Faxing Paper

**Commissioner for Patents**  
**P.O. Box 1450**  
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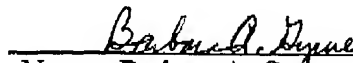
Applicants request issuance of a corrected Official Filing Receipt for the above-identified patent application. Although at the time of filing a large entity fee was paid, the entity is and has been a small entity. The filing receipt should claim small entity status as noted on the marked up version of the Official Filing Receipt.

In addition, the filing receipt should list the title of the application as "Recombinant Nematode Nicotinic Receptor and Uses" as indicated on page 1 of the Application filed on December 7, 2001 (copy enclosed). Please add to Filing Receipt in your proper manner.

A copy of the official Filing Receipt is enclosed with the corrections highlighted in red and underlined. It is believed that no further fees are due for this application.

Respectfully submitted,

Date:

June 16, 2004

Name: Barbara A. Gyure  
Registration No.: 34,614  
Palmer & Dodge LLP  
111 Huntington Avenue  
Boston, MA 02199-7613  
Tel: 617-239-0100



## UNITED STATES PATENT AND TRADEMARK OFFICE

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APPL NO.	FILING OR 371 (c) DATE	ART UNIT	FIL FEE REC'D	ATTY. DOCKET NO	DRAWINGS	TOT CLMS	IND CLMS
10/010,873	12/07/2001	1632	870	18396/2112	8	12	2

CONFIRMATION NO. 7464

UPDATED FILING RECEIPT



\*OC000000012237637\*

29933  
 PALMER & DODGE, LLP  
 KATHLEEN M. WILLIAMS  
 111 HUNTINGTON AVENUE  
 BOSTON, MA 02199

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## Applicant(s)

David Sattelle, Oxford, UNITED KINGDOM;  
 Emmanuel Culetto, Orsay, FRANCE;  
 Howard Baylis, Cambridge, UNITED KINGDOM; ✓

## Domestic Priority data as claimed by applicant

This application is a CIP of PCT/GB00/02270 06/09/2000

## Foreign Applications

UNITED KINGDOM GB99/13248.2 06/09/1999

If Required, Foreign Filing License Granted: 02/05/2002

Projected Publication Date: 07/08/2004

Non-Publication Request: No

Early Publication Request: No

Small Entity

Title

Recombinant nematode nicotinic receptor and uses

**Preliminary Class**

514

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Date of Deposit: December 7, 2001

Atty. Docket No.: 18396/2112

## Recombinant Nematode Nicotinic Receptor and Uses

### Introduction

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The nematode *C. elegans* has permitted identification and functional analysis of novel genes expressed in the nervous system (Bargmann, 1998). This invertebrate animal provides a highly effective genetic model with which to analyse *in vivo* molecules involved in chemical synaptic transmission (Jorgensen and Nonet 1995; Rand and Nonet 1997; Sattelle 1998). Neuromuscular cholinergic synapses in *C. elegans* have been analysed in detail stimulated by the finding that two major postsynaptic components, acetylcholinesterase (AChE, EC 3.1.1.7) and the nicotinic acetylcholine receptor (nAChR), are targets for widely used anthelmintic drugs. The hydrolytic enzymes AChEs which terminate the actions of ACh are inhibited by carbamates and organophosphates (Massoulié et al 1993). The nAChRs mediate the fast actions of the neurotransmitter ACh. When ACh binds to an nAChR molecule, the receptor molecule becomes transiently permeable to cations ( $\text{Na}^+$ ,  $\text{K}^+$ ,  $\text{Ca}^{2+}$ ). Anthelmintic drugs such as levamisole, pyrantel and morantel are agonists and open channel blockers at native nematode muscle nAChRs (Martin 1996). The studies to date of cholinergic anthelmintic actions on recombinant ACR-16 (=Ce21) homomeric (probably neuronal) nAChRs (Ballivet et al; Raymond et al 1999) do not mimic the actions observed on native nematode muscle nAChRs.

Five polypeptide subunits surround a central ion channel in each nAChR molecule, each polypeptide having four transmembrane regions (M1-4) and a large N-terminal extracellular domain containing residues that form the ACh binding sites (Karlin, 1993; Unwin 1993; Lena & Changeux 1998). These subunits are classified as either  $\alpha$  subunits, possessing two adjacent cysteines in loop C of the ACh binding site or non- $\alpha$  subunits, with no such adjacent cysteine motif.

Radioligand binding studies suggest the possibility of a diversity of nAChRs in *C. elegans*. For example, using [ $^3\text{H}$ ]meta-amino levamisole, a high saturable affinity binding activity has been observed and is regulated in the course of development, the highest binding activity being detected in larval stages (Lewis et